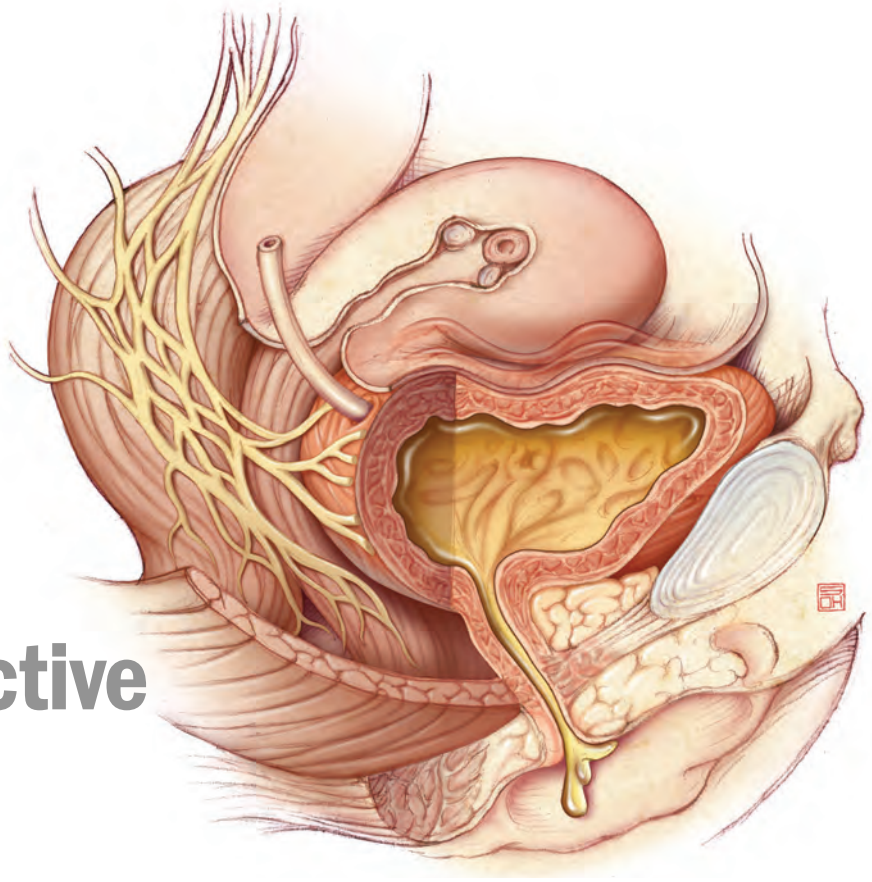

Overactive bladder in women

Achieving effective management

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The mainstay of treatment for women diagnosed with overactive bladder (OAB) is lifestyle and behavioural modification (bladder retraining) in combination with medical management such as anticholinergic therapy. Women with refractory OAB should be referred for further investigation and possible treatment with botulinum toxin type A injections or neuromodulation.

Urinary incontinence in women is a common problem with a community-based prevalence of 25%.[1] Although not life threatening, urinary incontinence impacts significantly on quality of life, with many women putting up with their symptoms for years or decades because of embarrassment and a perception that urinary incontinence is a normal part of ageing. The problem impacts on all spheres of life: domestic, occupational, physical, sexual, psychological and social. GPs are uniquely placed to screen for, investigate and initially manage women with this condition.

Urinary incontinence can be broadly divided into stress urinary incontinence (secondary to a weakness of the urethral sphincter) and urge urinary incontinence (secondary to overactive bladder [OAB]), although the two types often coexist (then termed 'mixed urinary incontinence'). This article will address the causes, investigation, diagnosis and management of women with OAB in the primary care setting and when to refer

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KEY POINTS

- Female urinary incontinence is a common problem with an estimated prevalence of 25%. Quality of life is significantly impacted by urinary incontinence, often leading to embarrassment and social isolation.
- Overactive bladder (OAB) denotes a symptom complex of urinary frequency and nocturia associated with urgency, a sudden compelling desire to void that cannot be deferred. It may or may not be associated with incontinence.
- It is important to exclude underlying pathology in women with OAB symptoms, including bladder malignancy, bladder foreign body and voiding dysfunction with overflow incontinence.
- Valuable investigations in a GP setting are a urinary diary, urine microscopy, culture and cytology, and an ultrasound scan of the bladder with postvoid residual volume.
- The mainstay of treatment is lifestyle and behavioural modification in combination with medical management such as anticholinergic therapy.
- Women with refractory OAB should be referred for further investigation with urodynamic studies and cystourethroscopy. Further management of these women includes the use of botulinum toxin type A intravesical injections or neuromodulation.

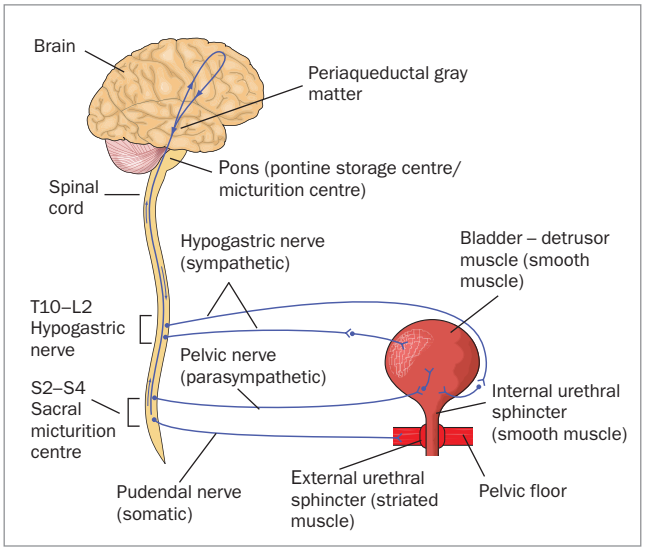


Figure 1. Neural control of the bladder (simplified).

these patients, and provide information on management options for those patients with refractory OAB.

What is overactive bladder?

OAB has been defined as urinary frequency and nocturia (nighttime voiding more than once per night) in the setting of urgency (a sudden, compelling desire to void that is difficult to defer) and in the absence of pathological or metabolic conditions that may explain the symptoms.[2] OAB may or may not result in urge urinary incontinence. Most women should be able to hold 300 to 500 mL of urine comfortably, voiding less than eight times during the day and less than twice at night.[3]

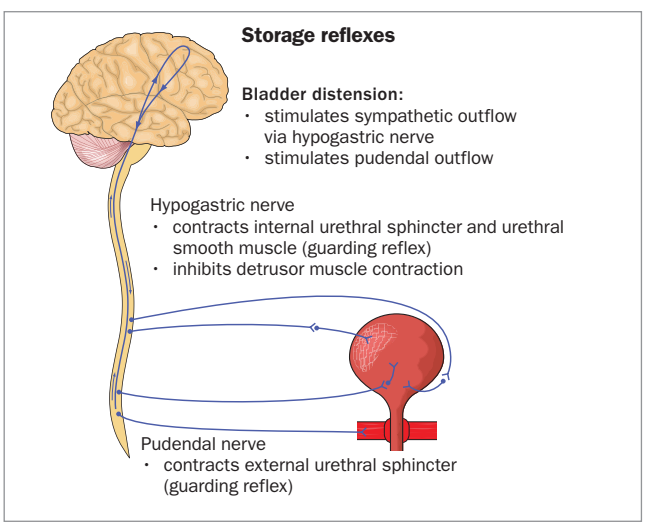
OAB is present in 12% of women in community-based studies.[4] Prevalence increases with age and it is the most common cause of urinary incontinence in the elderly population. OAB can be classified as neurogenic (secondary to a neurological condition such as stroke, Parkinson's disease, multiple sclerosis, spinal cord injury) and non-neurogenic (idiopathic, outlet obstruction).

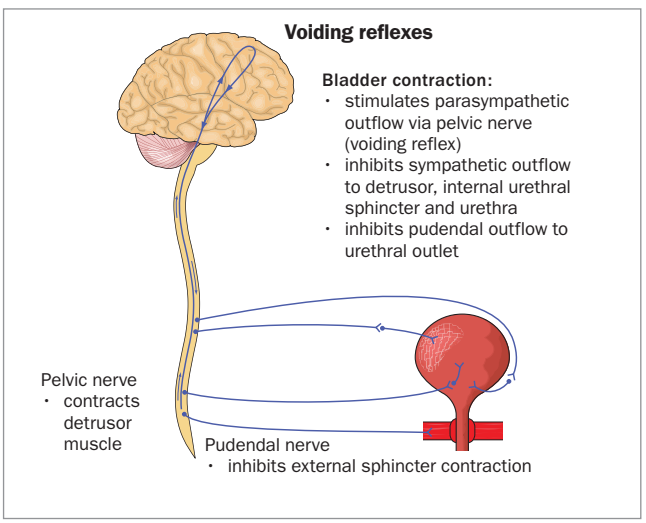
Pathogenesis of OAB

Normal bladder storage and emptying is facilitated by complex interactions between cortical (pontine micturition centre and periaqueductal gray matter) and subcortical (autonomic and somatic nervous systems) centres, as illustrated in Figures 1 and 2a and b.

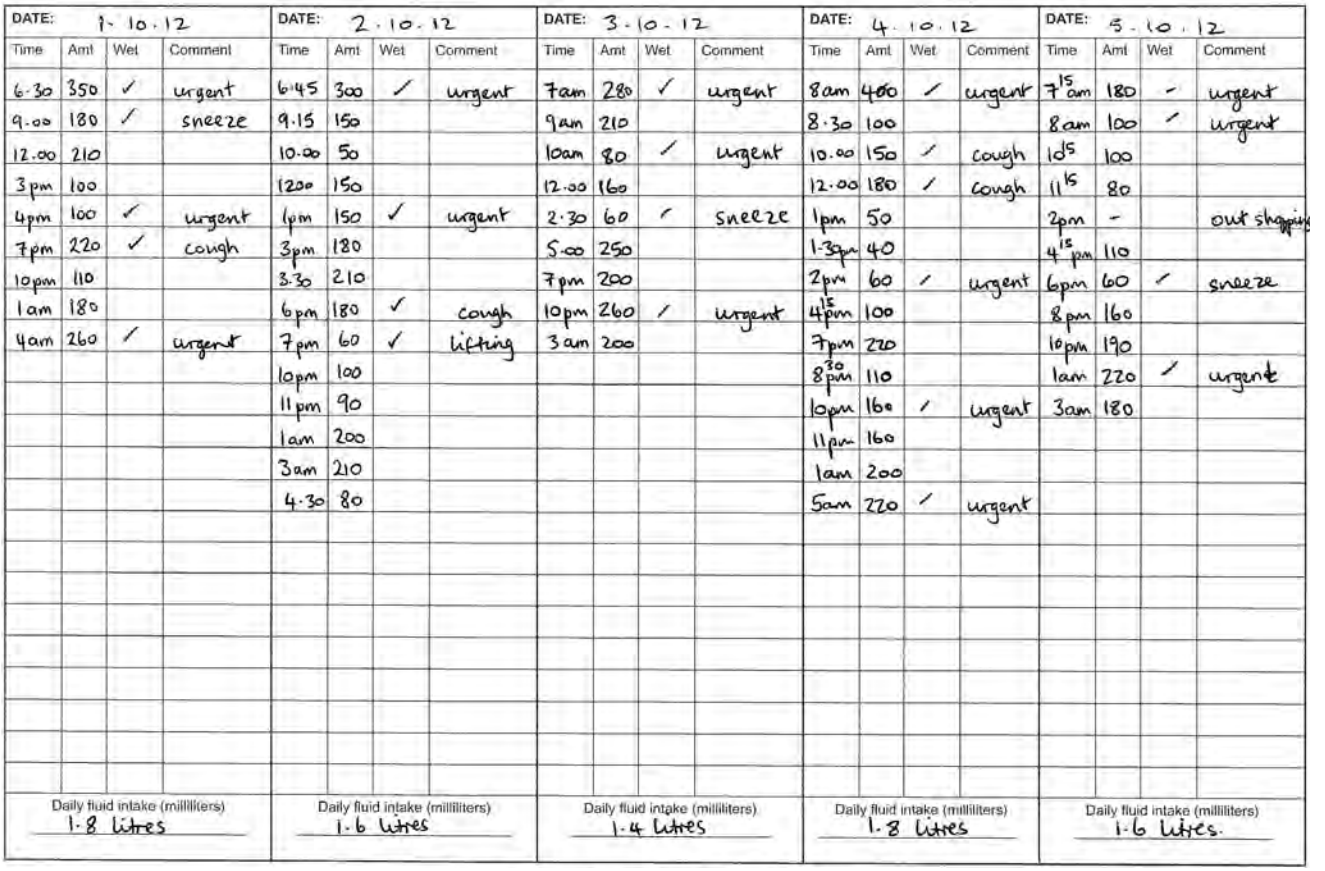
Storage is primarily a function of the sympathethic nervous system via the hypogastric nerve (T10 to L2). Bladder detrusor muscle relaxation occurs via the beta-adrenergic receptor β3 (thereby increasing bladder capacity), and bladder neck/urethral smooth muscle contraction occurs via alpha-adrenergic receptors. The somatic pudendal nerve (S2 to S4) innervates the external striated muscle of the urethra, resulting in further contraction and maintenance of continence.

Emptying involves stimulation of the parasympathetic nervous system (pelvic nerve, S2 to S4), with contraction of the detrusor muscle via M2 and M3 muscarinic acetylcholine receptors (the small population of M3 receptors is primarily responsible for detrusor contraction). Inhibition of sympathetic efferents and the pudendal nerve causes relaxation of the bladder neck and subsequent coordinated voiding. The pelvic floor muscles are innervated by branches from S2 to S4 nerve roots as well as the pudendal nerve. Adequate relaxation of the pelvic floor muscles





Figures 2a and b. Bladder storage and voiding reflexes. The storage (or 'guarding') reflexes promote continence; the voiding reflex and inhibition of the guarding reflexes allows elimination of urine.



DATE: 1-10-12			
Time	Amt	Wet	Comment
6·30	350	✓	urgent
9.00	180	✓	sneeze
12.00	210		
3pm	100		
4pm	100	✓	urgent
7pm	220	✓	cough
10pm	110		
1am	180		
4am	260	✓	urgent
Daily fluid intake (milliliters) 1·8 litres			

DATE: 2-10-12			
Time	Amt	Wet	Comment
6·45	300	✓	urgent
9.15	150		
10.00	50		
1200	150		
1pm	150	✓	urgent
3pm	180		
3.30	210		
6pm	180	✓	cough
7pm	60	✓	lifting
10pm	100		
11pm	90		
1am	200		
3am	210		
4.30	80		
Daily fluid intake (milliliters) 1·6 litres			

DATE: 3-10-12			
Time	Amt	Wet	Comment
7am	280	✓	urgent
9am	210		
10am	80	✓	urgent
12.00	160		
2·30	60	✓	sneeze
5.00	250		
7pm	200		
10pm	260	✓	urgent
3am	200		
Daily fluid intake (milliliters) 1·4 litres			

DATE: 4-10-12			
Time	Amt	Wet	Comment
8am	400	✓	urgent
8·30	100		
10.00	150	✓	cough
12.00	180	✓	cough
1pm	50		
1·3pm	40		
2pm	60	✓	urgent
4¹⁵pm	100		
7pm	220		
8³⁰pm	110		
10pm	160	✓	urgent
11pm	160		
1am	200		
5am	220	✓	urgent
Daily fluid intake (milliliters) 1·8 litres			

DATE: 5-10-12			
Time	Amt	Wet	Comment
7¹⁵am	180	-	urgent
8am	100	✓	urgent
10¹⁵	100		
11¹⁵	80		
2pm	-		out shopping
4¹⁵pm	110		
6pm	60	✓	sneeze
8pm	160		
10pm	190		
1am	220	✓	urgent
3am	180		
Daily fluid intake (milliliters) 1·6 litres.			

Figure 3. A completed bladder diary.

is required in order to achieve complete bladder emptying.

In OAB, increased bladder afferent activity is likely to contribute to the mechanisms leading to the subjective sensation of urgency and objective detrusor overactivity. Changes in urothelial receptor function and neurotransmitter release as well as increased excitability of detrusor smooth muscle cells leads to initiation of the micturition reflex at low levels of bladder filling.[5,6]

Diagnosis

History

Symptoms of OAB are easy to elicit from the patient. A screening question about urinary incontinence is asked first, and is followed by more detailed questioning to determine the type of urinary incontinence. Asking in what situations urine leakage occurs can determine whether the woman has stress urinary incontinence (occurring during coughing, sneezing, laughing or physical activity), OAB (with urgency, during hand washing or 'key in the door') or mixed urinary incontinence.

Conditions that may contribute to or mimic OAB include the following:

- voiding dysfunction leading to overflow incontinence – can present with OAB symptoms
- urinary tract infection – may lead to an acute exacerbation of OAB symptoms, or in women with refractory OAB, low-grade bacteriuria may contribute to aetiology in 35 to 40% of cases[7]
- bladder malignancy – may mimic OAB, and requires exclusion in patients at high risk, including those with a history of haematuria, smoking or occupational exposure to dyes
- foreign bodies in the bladder (stones, suture, mesh) – lead to irritative voiding symptoms similar to OAB; therefore, prior pelvic surgery should be documented
- bladder pain syndrome (also referred to as interstitial cystitis) – may mimic OAB, so should be considered in patients with urinary frequency/urgency symptoms and also bladder pain or discomfort.

Other factors that may impact on OAB symptoms include the following:

- fluid intake – both overall intake and type of fluid may have an impact on symptoms; history can be unreliable so objective documentation with a urinary diary is necessary.[8] Patients with OAB often significantly reduce their fluid intake in an attempt to decrease incontinence

episodes; concentrated urine, however, may exacerbate urgency
- caffeinated drinks – more than three caffeinated drinks a day may exacerbate urgency and frequency
- constipation
- uterovaginal prolapse – can contribute to lower urinary tract symptoms, so symptoms of bulge or protrusion should be enquired about
- past gynaecological or surgical history, including previous incontinence or prolapse surgery – may affect the patient's current symptomatology
- menopausal status and use of oestrogens (oral or topical) – should be documented
- diabetes or neurological disease
- use of antihypertensives combined with diuretics and of tricyclic antidepressants (due to their anticholinergic properties).

Examination

Assessment of mobility (ability to get to the toilet) can often be done during the history taking. Abdominal examination rarely identifies any pathology but should be performed to exclude the presence of a pelvic mass pressing on the bladder and resulting in OAB symptoms. Pelvic examination may reveal urethral prolapse and urogenital atrophy, stress incontinence or uterovaginal prolapse.

Investigation

A midstream urine analysis will identify any infection or haematuria. It is important to rule out voiding dysfunction and overflow incontinence underlying the patient's symptoms, and therefore an assessment of postvoid residual volume with a bladder scan, in/out catheter or post-micturition renal ultrasound should be performed. If the patient presents with haematuria or recurrent urinary tract infections, cystourethroscopy and urinary tract imaging with either ultrasound or CT intravenous pyelogram scan should be performed to detect any anatomical anomaly, stones or malignancy.

Asking the patient to complete a bladder diary provides valuable information regarding voiding frequency, functional bladder capacity, the number and type of incontinence episodes and fluid intake (Figure 3). The diary may cover a period of 24 hours to three days and provides objective evidence of the patient's bladder function during normal daily activities. In the general practice setting, a bladder diary will give a provisional diagnosis, and urodynamic testing is not routinely required.

Management

For patients with uncomplicated OAB, conservative management is the mainstay of treatment. Patients with persistent symptoms despite conservative measures or who have recurrent UTIs or haematuria should be referred for further investigation. The management of a woman with OAB is summarised in the flowchart.

Lifestyle/behavioural modification

Fluid intake

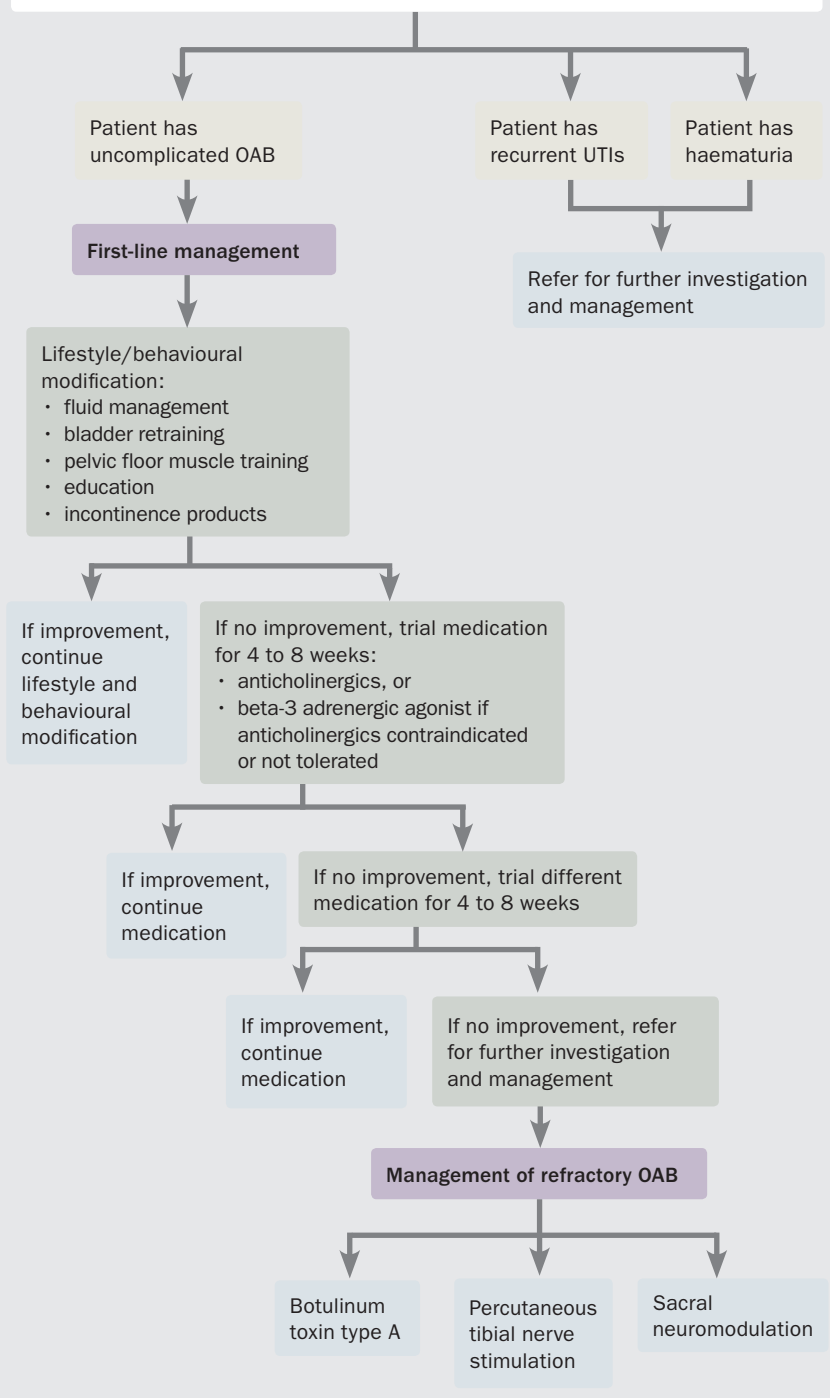
The initial focus should be on fluid intake. Aiming for 1.5 to 2 L of total fluid intake a day is a good starting point, and water should make up the majority of intake, with an emphasis on reducing caffeinated drinks and alcoholic beverages.

Bladder retraining

Bladder retraining is a key component of OAB management. Many patients demonstrate defensive voiding, going 'just in case' in an effort to reduce incontinence episodes. Over time, this contributes to a reduced functional capacity. The bladder diary will often show voided volumes of around 100 mL.

The aim of bladder retraining is to gradually increase the voiding interval, eventually aiming for two hours or longer between voids. For patients who void every 20 to 30 minutes, this can seem impossible. Initially, they may only be able to defer voiding for five to 10 minutes. Strategies to cope with urgency episodes, such as sitting down, crossing their legs, counting

AN APPROACH TO MANAGING WOMEN WITH OVERACTIVE BLADDER



Abbreviations: OAB = overactive bladder; UIT = urinary tract infection.

backwards from 100 or doing a few quick pelvic floor contractions, are simple and effective. Learning pelvic floor muscle training (pelvic floor exercises, also known as Kegel exercises) with a dedicated pelvic floor physiotherapist will also improve pelvic floor muscle tone and can help with concomitant stress urinary incontinence.

Constipation

Addressing constipation is important as this can impact on lower urinary tract symptoms. A rectum full of faeces may press on the bladder and limit filling capacity. Simple strategies such as increasing dietary fibre (aiming for 30 g/day) with psyllium husks or other fibre supplements are often all that is required. Stool softeners (docusate sodium) and osmotic laxatives (lactulose, macrogol 3350) benefit patients with more severe constipation. Stimulant laxatives with senna should be avoided because they are habituating.

Vulval health

Addressing vulval health is important. Many women use menstrual pads to contain their incontinence but these pads do not wick away the urine as effectively as incontinence products, often contributing to vulval irritant dermatitis. Using zinc-based barrier creams, avoiding the use of soap and wearing cotton underwear can all help to improve vulval symptoms.

For those patients with moderate to severe incontinence, the cost of incontinence products can be prohibitively expensive. The Federal Government has introduced a funding scheme that provides eligible patients with payments of around $500 per year to meet some of the costs of the incontinence products (Continence Aids Payment Scheme, www.bladderbowel.gov.au/caps/application.htm). State- and territory-based programs also exist to help with other continence aids, as listed on the Continence Foundation of Australia website (www.continence.org.au/pages/state-and-territory-schemes.html) and also others (e.g. the Victorian State-wide

OVERACTIVE BLADDER: RESOURCES FOR GENERAL PRACTITIONERS

- Continence Foundation of Australia
  www.continence.org.au
- Continence Aids Payment Scheme (CAPS), Australian Government Department of Human Services
  www.bladderbowel.gov.au/caps/application.htm
- State and Territory continence aids funding schemes
  www.continence.org.au/pages/state-and-territory-schemes.html
- State-wide Equipment Program (SWEP) – continence aids (Victoria)
  http://swep.bhs.org.au/continence-aids
- International Urogynecological Association (IUGA), patient information leaflets
  www.iuga.org/?page=patientinfo
- UroGynaecological Society of Australasia
  www.ugsa.org.au

TABLE. ANTICHOLINERGIC AND BETA-ADRENERGIC MEDICATIONS FOR OVERACTIVE BLADDER SYNDROME

Generic name	Dose	Mechanism of action
Oxybutynin 5 mg	2.5 to 5 mg three times daily	Nonselective muscarinic receptor antagonist
Oxybutynin 3.9 mg/day patch	One patch twice weekly	Nonselective muscarinic receptor antagonist
Tolterodine tartrate immediate release 1 or 2 mg	1 to 2 mg twice daily	Nonselective muscarinic receptor antagonist
Solifenacin 5 or 10 mg	5 or 10 mg daily	Selective M3 receptor antagonist
Darifenacin 7.5 or 15 mg	7.5 or 15 mg daily	Selective M3 receptor antagonist
Mirabegron 25 or 50 mg	25 or 50 mg daily	Beta-3 adrenergic receptor agonist

equipment program, http://swep.bhs.org.au/continence-aids). These and other useful resources are listed in the Box.

Restricted mobility may also impact on incontinence, particularly at night. Having a commode chair by the bed may be all that is required to reduce nocturnal urgency incontinence and reduce disruption to sleep.

Medications

Vaginal oestrogen therapy

Available data on animal studies supports the physiological role of oestrogen deficiency in OAB and the rationale for vaginal oestrogen therapy in postmenopausal patients with OAB. In a meta-analysis of 11 randomised, placebo-controlled trials, vaginal oestrogen was found to significantly reduce urgency compared with placebo.[9]

Topical oestrogen is preferable to oral administration as there is minimal systemic absorption and, as a result, no increased breast cancer risk and no significant effect on the endometrium. Patients can therefore be reassured that long-term treatment with vaginal oestrogen is safe and requires no endometrial protection. Despite this, it is prudent that prior to commencing vaginal oestrogen in those patients with a personal history of breast cancer, clearance is given from their breast surgeon or oncologist. The added benefit of using vaginal oestrogen is that it also deals with the symptoms of urogenital atrophy commonly present in patients with OAB, such as vaginal burning, dryness, itch and dyspareunia.

Anticholinergics

Anticholinergic (antimuscarinic) agents compete with acetylcholine at the muscarinic receptors in the detrusor muscle of the bladder and therefore depress normal bladder contractions. They can also affect muscarinic receptors at sites other than the bladder, causing side effects of dry mouth, dry eyes, blurred vision, constipation, drowsiness, cardiac arrhythmias and mental confusion in the elderly. Contraindications for anticholinergics include increased intraocular pressure associated with closed angle glaucoma (oxybutynin) and uncontrolled narrow angle glaucoma (darifenacin, solifenacin and tolterodine).

Several anticholinergic medications are available in Australia (Table). In general, they have all been found to be similarly effective in reducing frequency, urgency and urge incontinence episodes. Treatment effects of these agents, when compared with placebo, are modest due to the high placebo effect noted in the trials.[10,11] Side effects of blurred vision, dry mouth and constipation are common reasons for discontinuation.

The transdermal preparation of oxybutynin compared with the oral preparation avoids first-pass metabolism, has lower serum peak levels and therefore has lower rates of the anticholinergic side effects, although dermatitis at the site of adhesion can be problematic. Patients often try more than one anticholinergic medication before finding one that provides benefit with minimal side effects. Cost is also often a consideration as tolterodine, solifenacin and darifenacin are not included in the PBS.

Beta-3 adrenergic agonist

The β3-adrenergic receptor agonist mirabegron increases bladder capacity via activation of adenylate cyclase and formation of cAMP, which acts as an agonist at the β3-receptor, relaxing the detrusor muscle (unlike β1- and β2-adrenergic receptors, β3-receptors are not responsible for cardiovascular effects and therefore their stimulation does not have cardiovascular side effects). Studies have shown no effect on voiding parameters and minimal side effects,

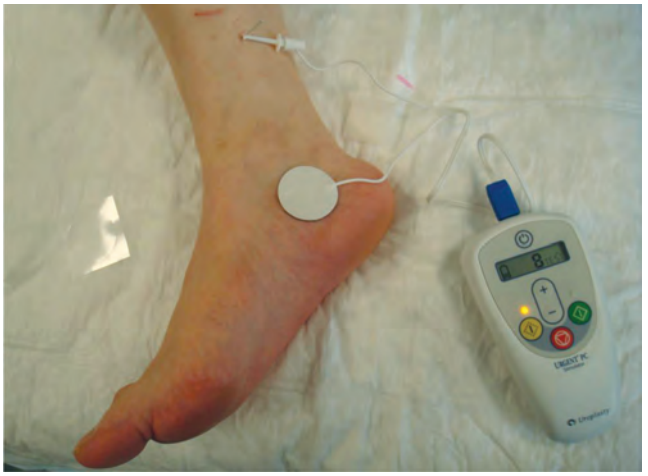


Figure 4. Percutaneous tibial nerve stimulation.

and mirabegron is therefore suitable as an alternative medication option for women in whom anticholinergics are contraindicated (i.e. those with narrow angle glaucoma) or not tolerated.[12,13]

Mirabegron has TGA approval for the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence in patients with OAB but is not included in the PBS.

What to do when simple measures fail?

Patients who remain symptomatic despite lifestyle modification and trials of anticholinergics or mirabegron have refractory OAB. These patients require referral for further investigation and are offered more invasive therapies.

Urodynamics

Urodynamic studies are undertaken when conservative measures fail or earlier in the investigation/treatment paradigm when patients present with more complex symptomatology (mixed urinary incontinence, previous incontinence or pelvic surgery, voiding dysfunction). Multichannel urodynamic studies give information about bladder capacity, bladder compliance, presence of detrusor overactivity and/or stress incontinence and voiding.

Multichannel urodynamic studies proceed through three phases. First, an uninstrumented free uroflow is obtained. This provides information on voided volume, flow rate and residual volume and can be used on its own as a screen for voiding dysfunction. Next, subtracted filling cystometry is performed with both vesical and rectal pressure catheters in situ. The patient's bladder is filled with water and information on detrusor pressures is obtained. During this filling phase, bladder compliance, the presence of spontaneous, unprovoked detrusor contractions (detrusor overactivity) and leak with cough and the Valsalva manoeuvre (urodynamic stress incontinence) are noted. Finally, the voiding pressure–flow study provides information on voiding pressures, which are particularly important in patients with voiding dysfunction.

Videourodynamics uses radiographic contrast instead of water for instillation and is performed with radiology to provide additional anatomical information about the bladder (i.e. presence of bladder diverticula, vesicoureteric reflux, bladder neck obstruction).

Cystourethroscopy is indicated in those patients with haematuria or prior pelvic surgery to exclude malignancy or a foreign body in the bladder.

Botulinum toxin type A injection

Botulinum toxin type A is PBS listed for use in both neurogenic and idiopathic OAB, provided at least two anticholinergic medications have been trialled and failed to control the patient's symptoms. It acts on both afferent and efferent neural pathways, decreasing acetylcholine release and down-regulating purigenic and capsaicin receptors, causing potent relaxation of smooth and striated muscle. Clinical trials have shown botulinum toxin A reduces urgency and incontinence episodes compared with placebo, and results in higher dry rates compared with anticholinergic medication (27% *vs* 13%; p=0.003).[14,15]

Botulinum toxin A is injected into the suburothelium or detrusor muscle during cystoscopy under local or general anaesthetic. For PBS subsidy, it can only be administered by a urogynaecologist or urologist accredited under the PBS. Dosing ranges from 100 to 200 units, with higher doses primarily used in neurogenic OAB. Effects can be seen from one to two weeks following injection, and return to baseline symptoms usually occurs between six and nine months following administration. Repeat injections appear to remain safe and effective. Complications such as procedure-related urinary tract infection (up to 30%) and voiding dysfunction (5 to 15%) are common. Voiding dysfunction may require short-term clean intermittent self-catheterisation until the effect of the botulinum toxin A starts to wear off.

Neuromodulation

The tibial nerve, a mixed sensory–motor nerve, originates in the L4 to S3 spinal roots and the peripheral nerves involved in the voiding bladder reflex originate in the sacral roots. Although the exact mechanism of action of neuromodulation is not fully understood, preferential stimulation of the S3 nerve root modulates the bladder reflex pathways at the spinal and supraspinal level. In patients with refractory OAB, stimulation of the afferent nerve fibres results in activation of inhibitory sympathetic neurons, thereby resulting in inhibition of bladder activity.

Percutaneous tibial nerve stimulation

Percutaneous tibial nerve stimulation (PTNS) was first described by McGuire in 1983.[16] It is performed on an outpatient basis

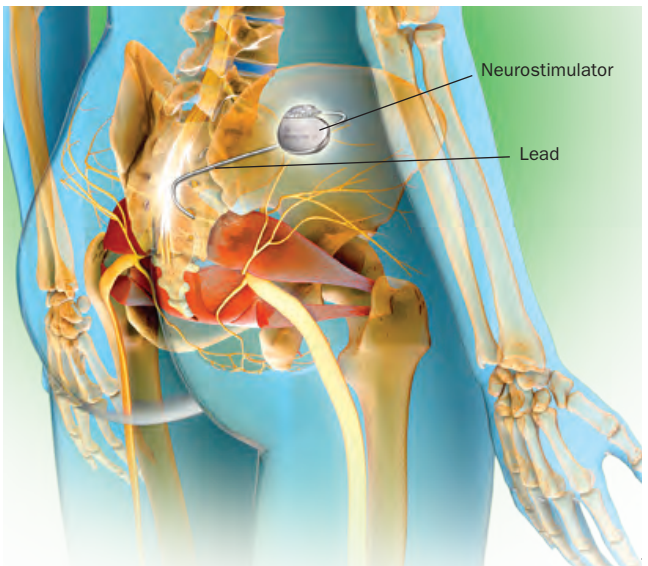


Figure 5. Sacral neuromodulation. Mild electrical pulses generated by the neurostimulator implanted in the buttock are delivered via the lead to an area near the sacral nerves. Preferential stimulation of these nerves modulates the bladder reflex pathways controlling continence.

Courtesy of Medtronic. © Medtronic.

with an initial treatment phase followed by a maintenance course of treatment. It involves placing a stainless steel acupuncture needle 3 to 5 cm above the medial malleolus, between the posterior margin of the tibia and soleus muscle (Figure 4). The needle is then connected to a low voltage stimulator. The initial treatment phase consists of 12 once-weekly 30-minute sessions, followed by monthly maintenance treatments, although this can be tailored to the patient's response to treatment.

In a randomised controlled trial of PTNS versus sham therapy, moderate to marked improvement in bladder symptoms was seen in 54.5% of patients in the PTNS group compared with 20.9% in the sham group ($p<0.001$).[17] Over 90% of the patients showing improvement in the PTNS group showed sustained improvement with maintenance therapy for three years.[18]

Sacral neuromodulation (SNM)

Sacral neuromodulation is a percutaneous two-staged procedure usually performed under local anaesthetic. It is TGA-approved for patients with urge incontinence, urgency/frequency, non-obstructive urinary retention and faecal incontinence.

The procedure involves an initial test phase with placement in the S3 foramen of an electrode connected to a protable external pulse generator (stimulator), followed by the subcutaneous implantation of the pulse generator (Figure 5). The pulse generator is only implanted if there has been a 50% or greater improvement in symptoms from baseline during the test phase, which can last from two to four weeks.

SNM has been shown to result in dry rates of 56%, with a 90% or greater improvement in leakage episodes and pad usage in 75% and 85% of subjects respectively at six months.[19] Sustained improvement has been shown up to five years following implantation, with 68% of those with urge incontinence and 56% of those with urinary frequency reporting successful outcomes.[20] Modifications to the implantation technique over the past decade have resulted in reduced complications, particularly infection, lead migration and explantation rates.

Augmentation cystoplasty

Augmentation cystoplasty is reserved for those patients with OAB who have failed conservative and less invasive treatment, and is now rarely necessary. These patients have small, poorly compliant bladders, and augmentation cystoplasty is often performed in an effort to reduce the risk of sustained vesicoureteric reflux in the neurogenic patient. A bowel segment (most commonly the ileum) is attached to the bivalved bladder and results in a bladder with larger capacity and higher compliance.

Conclusion

OAB denotes a symptom complex of urinary frequency and nocturia associated with urgency, and often urinary incontinence (urge incontinence). Investigations in the general practice setting are completion of a bladder diary, urine microscopy, culture and cytology, and an ultrasound scan of the bladder with determination of postvoid residual volume to exclude underlying pathology including bladder malignancy, a foreign body in the bladder and voiding dysfunction with overflow incontinence.

Medical management is with bladder retraining and anticholinergic drugs. Women with refractory OAB should be referred for further investigation with urodynamic studies and cystourethroscopy. Further management options are botulinum toxin type A intravesical injections and neuromodulation. MT

References

A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

COMPETING INTERESTS: None.

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